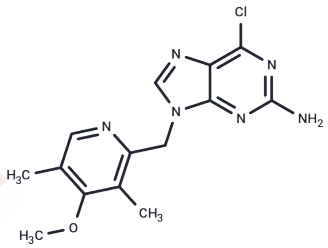
Data Sheet (Cat.No.T2286)

TargetMol

BIIB021

Chemical Properties



CAS No. : 848695-25-0

Formula: C14H15ClN6O

Molecular Weight: 318.76

Storage: Powder: -20°C for 3 years | In solvent: -80°C for 1 year
Actual storage temperature shall be subject to the COA.

Biological Description

Description	BIIB021 (CNF2024) is an orally-available, fully synthetic inhibitor of HSP90(Ki=1.7 nM, EC50=38 nM).
Targets(IC50)	HSP,Autophagy
In vitro	In various transplant tumor models, oral administration of BIIB021 effectively inhibits tumor growth. Specifically, in L540cy tumors, BIIB021 (120 mg/kg) is capable of suppressing cell proliferation.
In vivo	BIIB021 effectively inhibits cell growth in various tumor cell lines (IC50=0.06-0.31 μM), including BT474, MCF-7, N87, HT29, H1650, H1299, H69, and H82. It also suppresses cell proliferation in Hodgkin's lymphoma cells (IC50=0.24-0.8 μM), such as KM-H2, L428, L540, L540cy, L591, L1236, and DEV. Additionally, BIIB021 induces the degradation of Hsp90 proteins (including HER-2, Akt, and Raf-1) and upregulates the expression of heat shock proteins Hsp70 and Hsp27.
Kinase Assay	Hsp90 Binding Assay: For fluorescence polarization competition measurements, the FITC-geldanamycin probe (20 nM) is reduced with 2 mM TCEP at room temperature for 3 hours, after which the solution is aliquoted and stored at -80 °C until used. Recombinant human Hsp90α (0.8 nM) and reduced FITC-geldanamycin (2 nM) are incubated in a 96-well microplate at room temperature for 3 hours in the presence of assay buffer containing 20 mM HEPES (pH 7.4), 50 mM KCl, 5 mM MgCl2, 20 mM Na2MoO4, 2 mM DTT, 0.1 mg/mL BGG, and 0.1% (v/v) CHAPS. Following this preincubation, BIIB021 in 100% DMSO is then added to final concentrations of 0.2 nM to 10 μM (final volume 100 μL, 2% DMSO). The reaction is incubated for 16 hours at room temperature and fluorescence is then measured in an Analyst plate reader, excitation = 485 nm, emission = 535 nm. High and low controls contained no BIIB021 or no Hsp90, respectively. The data are fit to a four-parameter curve and IC50 is generated.
Cell Research	A modified tetrazolium salt assay is used to measure the IC50. Tumor cells are added to 96-well plates and propagated for 24 hours before BIIB021 addition. BIIB021 is added to the plated cells. DMSO (0.03-0.003%) is included as a vehicle control. After incubation phenazine methosulfate (stock concentration 1 mg/mL) and 3-(4,5-dimethylthiazol-2-yl)-5-(3-carboxymethoxyphenyl)-2-(4-sulfophenyl)-2H-tetrazolium, inner salt (stock concentration 2 mg/mL) are mixed at a ratio of 1:20 and added to each well of a 96-well plate. Reduction of 3-(4,5-dimethylthiazol-2-yl)-5-(3-carboxymethoxyphenyl)-2-(4-sulfophenyl)-2H-tetrazolium, inner salt gives rise to a soluble formazan product that is

Cell Research	secreted into the culture medium. After 4 hours incubation, the formazan product is quantitated spectrophotometrically at a wavelength of 490 nm. Data are acquired using SOFTmaxPRO software, and 100% viability is defined as the A490 of DMSO-treated cells stained with 3-(4,5-dimethylthiazol-2-yl)-5-(3-carboxymethoxyphenyl)-2-(4-sulfophenyl)-2H-tetrazolium, inner salt (the mean A490 of cells treated with DMSO at a range of 0.03-0.003%). Percent viability of each sample is calculated from the A490 values as follows: % viability = (A490 nm sample / A490 nm DMSO-treated cells × 100). The IC50 is defined as the concentration that gives rise to 50% inhibition of cell viabilit (Only for Reference)

Solubility Information

Solubility	DMSO: 125 mg/mL (392.14 mM),Sonication is recommended. (< 1 mg/ml refers to the product slightly soluble or insoluble)
In vivo Formulation	10% DMSO+40% PEG300+5% Tween 80+45% Saline: 2 mg/mL (6.27 mM),Sonication is recommended. *Please add the solvents sequentially, clarifying the solution as much as possible before adding the next one. Dissolve by heating and/or sonication if necessary. Working solution is recommended to be prepared and used immediately. The formulation provided above is for reference purposes only. In vivo formulations may vary and should be modified based on specific experimental conditions.*

Preparing Stock Solutions

	1mg	5mg	10mg
1 mM	3.1372 mL	15.6858 mL	31.3716 mL
5 mM	0.6274 mL	3.1372 mL	6.2743 mL
10 mM	0.3137 mL	1.5686 mL	3.1372 mL
50 mM	0.0627 mL	0.3137 mL	0.6274 mL

Please select the appropriate solvent to prepare the stock solution, according to the solubility of the product in different solvents. Please use it as soon as possible.

Note: The dilution table applies only to solid products. For liquid products, please calculate the stock solution based on the stated concentration and/or density.

Reference

Lundgren K, et al. Mol Cancer Ther, 2009, 8(4), 921-929.
Böll B, et al. Clin Cancer Res, 2009, 15(16), 5108-5116.
Yin X, et al. Int J Cancer, 2010, 126(5), 1216-1225.
Zhang H, et al. Int J Cancer, 2010, 126(5), 1226-1234.